The Global Burden of Dengue: A systematic analysis from the Global Burden of Disease Study 2013

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Abstract

Background:
We present estimates of dengue mortality, incidence and burden from the Global Burden of Disease study 2013, and the underlying methods used to produce them.

Methods:
We modelled mortality from vital registration, verbal autopsy and surveillance data using the Cause of Death Ensemble Modelling tool. We modelled incidence from officially reported cases, and adjusted our raw estimates for underreporting based on published estimates of expansion factors. In total, we had 1,780 country-years of mortality data from 130 countries, 1,636 country-years of dengue case reports from 76 countries, and expansion factor estimates for 14 countries.

Findings:
We estimated an average of 9,221 dengue deaths per year between 1990 and 2013, increasing from a low of 8,277 (5,353 – 10,649) in 1992 to a peak of 11,302 (6,790 – 13,722) in 2010. This yielded a total of 577 thousand (330 – 701 thousand) years of life lost to premature mortality (YLLs) attributable to dengue in 2013. Our model suggests a dramatic increase in the incidence of dengue between 1990 and 2013, with the number of cases more than doubling every decade, from 8·3 million (3·3 – 17·2) apparent cases in 1990 to 58·4 million (23·6 – 121·9) apparent cases in 2013. When accounting for disability from moderate and severe acute dengue, and post-dengue chronic fatigue, a total of 566 thousand (186 – 1,415 thousand) YLDs were attributable to dengue in 2013. Considering both fatal and non-fatal outcomes together, dengue was responsible for 1·14 million (0·73 – 1·98 million) DALYs in 2013.

Interpretation:
Though lower than other recently published estimates, our results offer more evidence that the true symptomatic incidence likely falls within the commonly cited range of 50 to 100 million annual cases. Our mortality estimates are lower than those presented elsewhere and should be evaluated in light of the totality of evidence suggesting that dengue mortality may, in fact, be substantially higher.

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Background

Dengue is the most common arbovirus infection globally, with transmission occurring in at least 128 countries and as many as 3·97 billion people at risk.[1] The number of dengue cases reported to the World Health Organization (WHO) has increased steadily from an average of less than a thousand annual cases globally in the 1950's to more than 3 million reported cases in 2013.[2–5] These reports, however, dramatically understate the problem and estimates of the true number of annual apparent infections range from 50 – 200 million, where apparent infections are defined as all symptomatic infections, including those that are undetected by reporting systems. The most commonly cited figures, and those recently cited by WHO, range from 50 – 100 million apparent cases annually.[6,7] While estimates of dengue deaths are less often reported, the most commonly cited figures are around 20 thousand annual dengue deaths.[8] To our knowledge, these figures seem to be largely based on expert opinion. The Global Burden of Disease (GBD) 2010 – providing the most recent data-driven estimate of dengue deaths of which we are aware – estimated over 14 thousand dengue deaths globally in 2010.[9]

The disparity between the number of reported cases and estimates of the number of true cases stems from under-recognition and under-reporting of dengue. Symptomatic dengue infections have a broad range of severity and as many as 70% may choose to not seek treatment or self-treat.[7] Even among those that are seen by a healthcare professional, clinical presentation of dengue shares similarities with up to 12 major pathogens making misdiagnosis common, particularly in areas with high incidence of febrile illnesses.[10] Population-based cohort studies have consistently found dengue cases to be dramatically underreported through official passive surveillance and reporting systems.[11,12] A number of studies have attempted to quantify the degree of underreporting by comparing incidence rates derived from active febrile-illness surveillance to comparable incidence rates derived from official reports. The ratio of these rates is referred to as an *expansion factor*, and it represents the number by which one would multiply the number of reported cases to derive the number of true apparent dengue infections in a given population. That said, the degree to which dengue is underreported varies by orders of magnitude across time and space, precluding the use of a simple multiplier. Moreover, many countries where dengue is believed to occur file no official reports, or do so only intermittently, and in these cases we would have no number of reported cases to which we could apply a multiplier.

Attempts to estimate the true incidence of symptomatic dengue must, therefore, address these problems. Bhatt et al [7] applied geostatistical methods to the problem: they first developed a global dengue risk map, then geolocated studies of dengue incidence and, finally, modelled the relationship between risk and incidence to estimate incidence for each 5 by 5 kilometer area. Their method yielded an estimate of 96 million (67 – 136 million) apparent infections globally. Unfortunately, this method cannot be easily made to estimate changes in dengue incidence over time.

Beyond incidence and mortality, understanding the true burden of dengue demands estimating metrics that allow for meaningful comparisons to other diseases that may differ in severity and duration, and that allow for comparisons between fatal and non-fatal outcomes. Among the most common of these burden metrics are years of life lost to premature mortality (YLL), which quantifies health loss due to mortality, giving greater weight to deaths occurring at younger ages; years lived with disability (YLD), which quantifies non-fatal health loss accounting for both the severity and duration of a given condition; and disability-adjusted life years (DALY), which captures the combination of YLLs and YLDs.

Here we present estimates of dengue mortality, incidence and burden by age, sex, and country, as estimated for the Global Burden of Disease Study (GBD) 2013. The Global Burden of Disease Study (GBD) 2013 was an effort to comprehensively and systematically estimate death and disability from 306 causes, producing estimates by year, age category (early neonatal, late neonatal, post neonatal, 1–4 years, five-year categories from age 5 through 79, and 80 or older), sex and country for the period from 1990 through 2013. While summary results have been published previously [13–15], here we present previously unpublished details of our modelling approach and results for dengue and discuss these results in the context of independent attempts to estimate the burden of dengue, with reference to dengue-specific literature.

Methods

Death estimation

The GBD Cause of Death (CoD) database, contains data on 240 causes of death and was built specifically for the GBD study from a combination of publicly available and restricted sources, including vital registration, verbal autopsy, and, surveillance data. The raw data were processed to reconcile disparate coding schemes (e.g. ICD-9, ICD-10), and redistribute "garbage codes", among other corrections.[15] We modelled dengue mortality using data in the CoD database and the Cause of Death Ensemble Modelling tool (CODEm) that has been described elsewhere.[15,16] Briefly, we selected covariates based on expected associations with dengue mortality and biological plausibility. Among these covariates, we included environmental variables (rainfall, proportion of the population living between 15°N and 15°S latitude, the proportion of the population living under 100 meters elevation, and the proportion of the population living in urban areas), and variables related to each country's level of development (lag-distributed income per capita, health system access, and mean years of education). Finally we included the population weighted mean probability of dengue transmission derived from Bhatt et al.[7] The full list of covariates, and the number of CODEm sub-models in which each covariate was used, is given in Appendix A.1. Within the GBD Study, all-cause mortality is estimated first and then, within each age-sex-country-year group, the sum of all cause-specific death estimates are constrained to equal the number of all-cause deaths through a process called CodCorrect.[15]

Incidence estimation

We attempted to correct for underreporting using a three-phase modelling approach. First, we defined the expected spatial distribution of disease, based on a principal components analysis of the population-weighted probability of dengue transmission and our model-based estimates of dengue mortality. Second, we modelled the association between this expected distribution and reported incidence, using mixed-effects negative binomial model, with the assumption that deviations from the expected distribution reflect deviations in completeness of reporting. And, third, we calibrated the model by benchmarking these deviations against published empirical expansion factors (see Appendix A.2 for details). The case reports used in this analysis do not disaggregate cases by age and sex. We therefore modelled total cases by country and year and then distributed cases to age-sex groups based on the age-sex distribution of dengue cases captured by the Hospital Information System of the Brazilian Unified National Health System (SIH-SUS).

Burden estimation

We estimated three burden metrics: years of life lost to premature mortality (YLL), years lived with disability (YLD) and disability adjusted life years (DALY). YLLs were estimated as the difference between the age of death and the corresponding life expectancy goal for those surviving to that age of death; here, the life-expectancy goal is based on a theoretical composite life table in which the target life-expectancy for each age is equal to the longest observed life-expectancy among people of that age in any country.[15] YLDs were calculated as the product of the number of cases having a given health state, the duration of that health state, and the disability weight for that health state. DALYs were calculated as the sum of YLLs and YLDs. To estimate years lived with disability (YLD), we assigned a health state and corresponding disability weight to each case. Disability weights were based on pooled results from the GBD 2010 Disability Weights Measurement study [17] and the more recent European disability weights study [18]. We assigned each dengue case to one of two acute health states: 94·5% of cases were assigned the disability weight for "infectious disease, acute episode, moderate" with a mean duration of 6 days; and 5·5% were assigned the disability weight for "infectious disease, acute episode, severe" with a mean duration of 14 days.[19] We derived the proportions for the split between moderate and severe states based on a meta-analysis of the subset of case notification data that presented both the total number of cases, and the number of severe cases (defined as either dengue hemorrhagic fever or dengue shock syndrome). Note that our definition of "severe" is intended to correspond to the definition of a severe acute infectious disease episode within the context of disability weights, and does not correspond to the WHO's current definition of "severe dengue."[20] Additionally, 8·5% of cases were assumed to experience post-dengue chronic fatigue, and assigned the disability weight for "Infectious disease, post-acute consequences", with a mean duration of six-months.[21]

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

We estimated an average of 9,221 dengue deaths per year between 1990 and 2013, increasing from a low of 8,277 (5,353 – 10,649) in 1992 to a peak of 11,302 (6,790 – 13,722) in 2010. Mortality rates were highest among those under one-year of age, declined with age into adulthood, and increased with age over 45 years. A slightly larger proportion of dengue deaths occurred among females (51·5%) than males (Table 1). The majority of dengue deaths, and the highest dengue mortality rates occurred in the Southeast Asia region (Figure 1). We estimated a total of 577 thousand (330 – 701 thousand) YLLs attributable to dengue in 2013 (Table 2).

Our model suggests a dramatic increase in the incidence of dengue between 1990 and 2013, with the number of cases more than doubling every decade, from 8·3 million (3·3 – 17·2) apparent cases in 1990 to 58·4 million (23·6 – 121·9) apparent cases in 2013 (Table 3). We estimated a global mean expansion factor of 12·3 (6·7 – 20·8), meaning that, where we have official case reports, we believe that those reports capture an average of only 8% of symptomatic dengue infections. The highest age-standardized incidence rates occur in Southeast Asia, with an annual average of 34·3 (12·7 – 75·0) cases per thousand people in the region (Figure 2). A total of 566 thousand (186 – 1,415 thousand) YLDs were attributable to dengue in 2013, with post-infection chronic fatigue accounting for the majority of this disability: 7·8%, 2·9% and 89·9% of YLDs were from moderate acute infection, severe acute infection and chronic fatigue, respectively.

Considering both fatal and non-fatal outcomes together, dengue was responsible for 1·14 million (0·73 – 1·98 million) DALYs in 2013, representing a 58% increase from the 0·72 million (0·43 – 0·95 million) DALYs estimated for 1990 (Table 2 and Figure 3). Given the stronger trend in our incidence than mortality estimates, YLDs accounted for an increasing proportion of DALYs in later years: the proportion of DALYs from YLDs increased from 11·1 to 49·5% from 1990 to 2013, while the proportion from YLLs decreased from 88·9 to 50·5% during that period.

Discussion

Our results suggest that there are about 58·4 million (95% UI: 26·6 -121·9 million) annual symptomatic dengue infections resulting in about 10 thousand deaths per year. Our results, furthermore, suggest a dramatic increase in the incidence of dengue in the past two decades, with the number of symptomatic dengue infections more-than doubling every ten years between 1990 and 2013. In addition to this long-term secular trend, dengue occurs in both seasonal and interannual cycles that are obscured by the course temporal resolution of our estimates. The highest dengue incidence and mortality occurs in Southeast Asia, where severe dengue is one of the leading causes of hospitalization and death among children.[22] Overall, our findings underscore the growing disease burden of dengue to people and health systems in most tropical and subtropical countries globally.

Our mean estimate of dengue incidence for 2013 is lower than the recent estimates from Bhatt et al of 96 million apparent infections in 2010. Given the wide uncertainty in both estimates, however, the two estimates are not statistically significantly different and their estimate falls within our 95% uncertainty interval of 26·6 to 121·9 million cases. Interestingly, these two approaches have yielded results that bracket the commonly cited range of 50-100 million cases and offer more evidence that the true incidence likely falls within that range. Comparing regional estimates, our estimate of 5·9 million annual dengue cases in the Americas is comparable to the Shepard et al. estimate of 5·6 million cases in the Americas per year in 2000 through 2007.[23] However, our estimate of 21·1 million cases in Southeast Asia is notably higher than the Undurraga et al. estimate of 2·9 million per year for 12 countries in Southeast Asia in 2001 through 2010. [11] This difference is driven mainly by estimates for Indonesia, Malaysia, and the Philippines, but the overall difference is probably explained by a combination of limited available evidence at the time of the study, inadequate surveillance and substantial underreporting, and an increase in dengue incidence in the past years.

Two multi-country vaccine trials were recently published, one in Southeast Asia and one in Latin America. The dengue incidence observed in the control arms of these trials offer new data against which to validate our model-based estimates for nine countries, though differences in age categorization and the study years preclude a perfect comparison. Villar et al[24] studied Latin American children ages 9 to 16, from 2011 through 2013; we compared incidence observed in the trial to GBD estimates among children ages 10 through 14 in 2013. Our estimates are consistently lower than the observed incidence for all four Latin American countries, though our uncertainty intervals cover the trial estimate for Honduras (Figure 4). This is not terribly surprising given the diversity of dengue risk within large countries like Mexico and Brazil, and the preference to conduct trials in those parts of a country where risk is greatest. Capeding et al[25] studied children between 2 and 14 years of age in five Southeast Asian countries, collecting data primarily in 2012. We compared incidence observed in the trial to GBD estimates among children ages 1 through 14 in 2013. For all five countries, GBD and trial-based uncertainty intervals overlapped; and for all countries except Thailand, GBD uncertainty intervals covered the trial-based point estimate (Figure 4).

Our estimates of the number of annual dengue deaths ranged from 8,365 to 10,394, lower than commonly cited figures of approximately 20 thousand. Our mortality estimates are also lower than those for GBD 2010, though the differences are not statistically significant. Much of the change in mortality estimates between GBD 2010 and GBD 2013 is driven by new data that suggest lower dengue mortality in some countries: newly acquired detailed subnational mortality data from China is the most notable example, and with an average of 881 fewer cases per year estimated for the period from 1990 through 2010, China's estimates changed more than those for any other country. Notably, compared to GBD 2010, our model estimates an average of about 2,300 fewer dengue deaths in non-endemic countries. This change is driven by a combination of new data and improved covariates, most notably the newly added population-weighted probability of dengue transmission variable. Looking at the period from 1990 through 2010, the total number of estimated deaths in dengue endemic countries declined by a statistically insignificant total of 250 deaths annually between GBD 2010 and GBD 2013. The important data gaps that exist for several large, high-incidence countries (e.g. Indonesia) suggest that our mortality estimates should be interpreted with caution, and evaluated in light of the totality of evidence suggesting that dengue mortality may, in fact, be substantially higher. This is a limitation that we hope to address in future GBD revisions by acquiring additional data from other dengue endemic countries.

Despite the strong internal consistency between our incidence and mortality estimates with regard to spatial distribution, we note that the temporal trends in these two sets of estimates are quite different. While our estimates of incidence show a strong increasing trend, the trend in our mortality estimates is less clear and far less powerful. It is worth noting that our incidence model cannot differentiate true increases in incidence from increases in reporting. If we assume, however, that dengue has, in fact, become more frequent, there are two possible explanations for our relatively flat mortality estimates. First, case-fatality may be declining due to better clinical management of severe cases, changing numbers of average lifetime infections, or changing mortality risk due to changing age distribution of infections, a phenomenon known as endemic stability.[26] Indeed PAHO reported a 29% decline in case-fatality in the Americas between 2010 and 2013, suggesting that this is a plausible explanation.[27] Second, gaps in dengue mortality data – most notably in high-incidence countries in Southeast Asia – may limit our ability to reliably estimate trends. It seems likely that both factors are contributing, at least to some degree, to our estimated mortality trends and this issue will require further attention in future iterations of the GBD Study.

The main strength of our results derives from combining multiple data sources and available evidence on dengue incidence and deaths, including the probability of dengue occurrence, adjustments for underreporting, and a substantial refinement in our models to estimate dengue incidence and mortality rates. The main limitation relates to the limited availability and quality of surveillance data in many dengue endemic countries, mostly including Africa and South Asia. Moreover, use made use of verbal autopsy (VA) data in our mortality estimates. While this accounted for only 0.19% of our mortality data, it should be noted that VA is an imperfect method for assigning deaths, especially for diseases like dengue that typically lack localizing signs. Recent evidence suggests there might be substantial underreporting of fatal dengue episodes even in relatively well-funded health systems,[28] and possibly misdiagnosis in countries with other predominant febrile illness such as malaria.[29] Seasonal variations in transmission, dengue severity, accessibility to healthcare, improvements in surveillance systems, and also, the fact that dengue is becoming a reportable disease in an increasing number of countries, all influence the extent to which dengue is underreported in any given country and year. New studies of underreporting of dengue have been published that were not included in our model, and we expect to include more evidence on our next round of estimates. Conversely, over-reporting in some areas – most notably during epidemics – may also occur, and we lack adequate expansion factor data to address this potential issue. That said, we believe that, if such over-reporting occurs, the overall effect should be minor.[30] Finally, our DALY estimates do not capture several unique societal burdens of dengue. Its extreme year-to-year variability and potential for rapid onset of severe disease create fear in endemic areas, precautionary hospitalization, health system congestion during outbreaks, and risk of damaging tourist economies.

We found limited age-specific data on dengue incidence. In the absence of better data, the age distribution that we imposed on cases represents a crude approximation. The true age distribution in a given country and year will be driven primarily by the overall force of infection and acquisition of immunity, with a higher force of infection producing an age pattern shifted toward younger age groups. With the prospect of a dengue vaccine, accurate age-specific estimates may become increasingly important for understanding the implications of vaccine use recommendations. We hope to address this shortcoming in future revisions of the GBD study. Future work will refine these expected age distributions by taking into account an area's force of infection (as measured by age-stratified seroprevalence surveys), serotype history and different theories of acquisition of type-specific and heterologous immunity.[31]

Finally, the overall magnitude of dengue incidence is calibrated against expansion factor data. As we have expansion factor estimates from only 14 countries, this may represent the weakest evidential link in our modelling chain. Accordingly, we have propagated uncertainty from these expansion factors into our final estimates, and uncertainty in these expansion factors represents the largest single source of uncertainty in our final incidence estimates. We believe that the resulting uncertainty intervals around our case estimates for recent years accurately reflect the uncertainty in these estimates. However, given our modelling approach, the widths of these uncertainty intervals are relative to the magnitude of point estimate, and are thus narrower for earlier years where our incidence estimates are lower. It is likely, then, that the uncertainty intervals for case estimates for earlier years underestimate the true uncertainty in those estimates.

Dengue is among the diseases with the highest increase in age-standardized incidence rates between 1990 and 2013, which counters the global trend away from communicable diseases. The results presented here constitute one of the most comprehensive efforts to quantify the burden of dengue in countries with evidence of ongoing dengue transmission. The methods represent a major improvement compared to those used in GBD 2010, and we expect to keep updating and improving their accuracy. Our hope is that these improved estimates of dengue incidence and mortality, and their longer term trend, will inform public health officials, scholars, and policy makers to assess and identify cost-effective control strategies to reduce the dengue transmission and disease burden.

References

1 Brady OJ, Gething PW, Bhatt S, *et al.* Refining the global spatial limits of dengue virus transmission by evidence-based consensus. *PLoS Negl Trop Dis* 2012; **6**: e1760.
2 DengueNet. WHO. http://www.who.int/csr/disease/dengue/denguenet/en/ (accessed April 24, 2015).
3 World Health Organization, | Vector borne and neglected tropical diseases. SEARO. http://www.searo.who.int/entity/vector_borne_tropical_diseases/en/ (accessed June 24, 2015).
4 PAHO. Number of Reported Cases of Dengue and Severe Dengue in the Americas, by Country. 2014; published online June 5. http://www.paho.org/hq/index.php?option=com_topics&view=readall&cid=3273&Itemid=40734&lang=en.
5 WPRO | Annual Dengue Data in the Western Pacific Region. WPRO. http://www.wpro.who.int/emerging_diseases/annual.dengue.data.wpr/en/ (accessed June 24, 2015).
6 Dengue. WHO. http://www.who.int/denguecontrol/en/ (accessed April 10, 2015).
7 Bhatt S, Gething PW, Brady OJ, *et al.* The global distribution and burden of dengue. *Nature* 2013; 496, 504–507. DOI:10.1038/nature12060.
8 Impact of Dengue. WHO. http://www.who.int/csr/disease/dengue/impact/en/ (accessed April 24, 2015).
9 Vos T, Flaxman AD, Naghavi M, *et al.* Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet* 2012; **380**: 2163–96.
10 Simmons CP, Farrar JJ, van Vinh Chau N, Wills B. Dengue. *N Engl J Med* 2012; **366**: 1423–32.
11 Undurraga EA, Halasa YA, Shepard DS. Use of Expansion Factors to Estimate the Burden of Dengue in Southeast Asia: A Systematic Analysis. *PLoS Negl Trop Dis* 2013; **7**: e2056.
12 Shepard DS, Undurraga EA, Betancourt-Cravioto M, *et al.* Approaches to refining estimates of global burden and economics of dengue. *PLoS Negl Trop Dis* 2014; **8**: e3306.
13 Murray, Christopher J L *et al.* Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. *Lancet* 2015. Advance online publication, August 26. DOI: 10.1016/S0140-6736(15)61340-X.
14 Vos, Theo *et al.* Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015, 386, 743-800.
15 GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet* 2015; **385**: 117–71.
16 Foreman KJ, Lozano R, Lopez AD, Murray CJ. Modeling causes of death: an integrated approach using CODEm. *Popul Health Metr* 2012; **10**: 1.
17 Salomon JA. New disability weights for the global burden of disease. *Bull World Health Organ* 2010; **88**: 879.
18 Haagsma JA, Noordhout CM de, Polinder S, *et al.* Assessing disability weights based on the responses of 30,660 people from four European countries. *Popul Health Metr* 2015; **13**: 10.

19 Whitehead SS, Blaney JE, Durbin AP, Murphy BR. Prospects for a dengue virus vaccine. *Nat Rev Microbiol* 2007; **5**: 518–28.
20 WHO. Dengue Guidelines for Diagnosis, Treatment, Prevention and Control, New edition. Geneva: World Health Organization, 2010.
21 Teixeira L de AS, Lopes JSM, Martins AG da C, Campos FAB, Miranzi S de SC, Nascentes GAN. Persistence of dengue symptoms in patients in Uberaba, Minas Gerais State, Brazil. *Cad Saúde Pública* 2010; **26**: 624–30.
22 Gubler DJ, Ooi EE, Vasudevan S, Farrar J, editors. Dengue and Dengue Hemorrhagic Fever, 2 edition. Wallingford, Oxfordshire ; Boston, MA: CABI, 2014.
23 Shepard DS, Coudeville L, Halasa YA, Zambrano B, Dayan GH. Economic Impact of Dengue Illness in the Americas. *Am J Trop Med Hyg* 2011; **84**: 200–7.
24 Villar L, Dayan GH, Arredondo-García JL, *et al.* Efficacy of a Tetravalent Dengue Vaccine in Children in Latin America. *New England Journal of Medicine* 2015; **372**: 113–23.
25 Capeding MR, Tran NH, Hadinegoro SRS, *et al.* Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial. *The Lancet* 2014; **384**: 1358–65.
26 Egger JR, Ooi EE, Kelly DW, Woolhouse ME, Davies CR, Coleman PG. Reconstructing historical changes in the force of infection of dengue fever in Singapore: implications for surveillance and control. *Bull World Health Organ* 2008; **86**: 187–96.
27 PAHO/WHO. Five-fold increase in dengue cases in the Americas over the past decade. 2014; published online May 29. http://www.paho.org/hq/index.php?option=com_content&view=article&id=9657%3Alos-casos-de-dengue-en-las-americas-se-quintuplicaron-en-diez-anos-segun-nuevos-datos-de-la-opsoms&Itemid=1926&lang=en (accessed April 14, 2015).
28 Tomashek KM. The Acute Febrile Illness Surveillance Study in Puerto Rico: Findings from the First Two Years. Idsa, 2014. https://idsa.confex.com/idsa/2014/webprogram/Paper47354.html (accessed June 24, 2015).
29 Senn N, Luang-Suarkia D, Manong D, Siba PM, McBride WJH. Contribution of dengue fever to the burden of acute febrile illnesses in Papua New Guinea: an age-specific prospective study. *Am J Trop Med Hyg* 2011; **85**: 132–7.
30 Chairulfatah A, Setiabudi D, Ridad A, Colebunders R. Clinical manifestations of dengue haemorrhagic fever in children in Bandung, Indonesia. *Ann Société Belge Médecine Trop* 1995; **75**: 291–5.
31 Imai N, Dorigatti I, Cauchemez S, Ferguson NM. Estimating Dengue Transmission Intensity from Sero-Prevalence Surveys in Multiple Countries. *PLoS Negl Trop Dis* 2015; **9**: e0003719.

Table 1: Dengue deaths and mortality rates (MR) per million, by sex, age, region, and World Bank income group for 1990 and 2013. 95% uncertainty intervals are given in parentheses.

	1990						2013					
	Deaths			**MR (per million)**			**Deaths**			**MR (per million)**		
Total	8,657	(5,484,	10,819)	1·64	(1·04,	2·04)	9,110	(5,630,	10,842)	1·27	(0·79,	1·52)
Sex												
Male	4,349	(2,516,	5,801)	1·63	(0·94,	2·18)	4,433	(2,515,	5,340)	1·23	(0·70,	1·48)
Female	4,308	(2,556,	5,611)	1·64	(0·97,	2·14)	4,677	(2,500,	5,723)	1·32	(0·71,	1·61)
Age												
Post Neonatal	978	(459,	1,417)	8·05	(3·78,	11·67)	650	(303,	899)	5·21	(2·43,	7·20)
1 to 4	3,016	(1,400,	4,449)	5·97	(2·77,	8·81)	1,967	(1,047,	2,761)	3·75	(2·00,	5·27)
5 to 9	1,828	(951,	2,437)	3·16	(1·65,	4·22)	1,568	(703,	2,117)	2·53	(1·13,	3·41)
10 to 14	595	(403,	725)	1·13	(0·76,	1·37)	711	(387,	862)	1·19	(0·65,	1·45)
15 to 19	276	(197,	313)	0·54	(0·38,	0·61)	378	(224,	449)	0·64	(0·38,	0·76)
20 to 24	273	(210,	326)	0·56	(0·43,	0·67)	389	(271,	473)	0·63	(0·44,	0·77)
25 to 29	291	(229,	359)	0·67	(0·52,	0·82)	448	(315,	545)	0·75	(0·53,	0·91)
30 to 34	263	(206,	331)	0·68	(0·53,	0·86)	420	(300,	506)	0·79	(0·57,	0·96)
35 to 39	222	(178,	280)	0·65	(0·52,	0·81)	369	(264,	456)	0·75	(0·54,	0·93)
40 to 44	187	(156,	244)	0·67	(0·56,	0·87)	355	(267,	431)	0·75	(0·56,	0·91)
45 to 49	99	(79,	114)	0·43	(0·34,	0·50)	233	(169,	263)	0·53	(0·39,	0·60)
50 to 54	99	(80,	117)	0·47	(0·38,	0·55)	232	(163,	261)	0·61	(0·43,	0·68)
55 to 59	89	(76,	110)	0·48	(0·41,	0·59)	218	(158,	247)	0·67	(0·49,	0·76)
60 to 64	96	(83,	123)	0·61	(0·52,	0·77)	229	(176,	263)	0·82	(0·63,	0·94)
65 to 69	97	(83,	133)	0·79	(0·67,	1·08)	224	(175,	265)	1·19	(0·93,	1·41)
70 to 74	78	(67,	101)	0·9	(0·77,	1·16)	199	(147,	237)	1·32	(0·97,	1·57)
75 to 79	60	(49,	70)	0·95	(0·78,	1·12)	158	(108,	178)	1·48	(1·01,	1·67)
80 plus	107	(78,	128)	1·89	(1·38,	2·26)	364	(252,	443)	3·03	(2·10,	3·69)
Super-region/Region												
Central Europe, Eastern Europe, and Central Asia												
Central Asia	20	(16,	22)	0·29	(0·23,	0·33)	15	(13,	19)	0·18	(0·15,	0·23)
Central Europe	66	(28,	76)	0·53	(0·23,	0·62)	12	(11,	19)	0·1	(0·09,	0·16)
Eastern Europe	25	(22,	35)	0·11	(0·10,	0·16)	22	(18,	30)	0·1	(0·09,	0·14)
High-income												
Australasia	2	(2,	3)	0·11	(0·10,	0·15)	3	(2,	3)	0·1	(0·07,	0·11)
High-income Asia Pacific	22	(20,	27)	0·13	(0·12,	0·16)	18	(14,	21)	0·1	(0·08,	0·12)
High-income North America	29	(27,	40)	0·11	(0·10,	0·14)	34	(26,	40)	0·1	(0·07,	0·11)
Southern Latin America	33	(26,	37)	0·67	(0·53,	0·75)	20	(16,	34)	0·33	(0·26,	0·55)
Western Europe	77	(50,	85)	0·2	(0·13,	0·22)	42	(35,	52)	0·1	(0·08,	0·12)
Latin America and Caribbean												
Andean Latin America	55	(47,	68)	1·42	(1·22,	1·77)	44	(35,	60)	0·77	(0·62,	1·05)
Caribbean	41	(36,	68)	1·35	(1·17,	2·21)	126	(51,	163)	3·24	(1·31,	4·18)
Central Latin America	118	(107,	172)	0·7	(0·64,	1·03)	259	(153,	301)	1·05	(0·62,	1·23)
Tropical Latin America	21	(18,	41)	0·14	(0·11,	0·26)	279	(41,	343)	1·35	(0·20,	1·66)
North Africa and Middle East												
North Africa and Middle East	110	(68,	131)	0·34	(0·21,	0·41)	72	(62,	89)	0·14	(0·12,	0·18)
South Asia												
South Asia	1,712	(1,328,	2,584)	1·54	(1·19,	2·32)	2,132	(1,741,	2,825)	1·29	(1·06,	1·71)
Southeast Asia, East Asia, and Oceania												
East Asia	242	(159,	320)	0·2	(0·13,	0·27)	144	(120,	167)	0·1	(0·08,	0·12)
Oceania	71	(53,	88)	12·1	(9·14,	15·03)	78	(57,	131)	8·13	(5·94,	13·64)
Southeast Asia	5,645	(2,727,	7,741)	12·4	(5·97,	16·95)	5,376	(2,494,	6,765)	8·49	(3·94,	10·68)
Sub-Saharan Africa												
Central Sub-Saharan Africa	42	(21,	62)	0·81	(0·40,	1·18)	62	(39,	89)	0·62	(0·38,	0·88)
Eastern Sub-Saharan Africa	46	(37,	60)	0·25	(0·20,	0·32)	66	(53,	81)	0·18	(0·15,	0·23)
Southern Sub-Saharan Africa	19	(6,	23)	0·36	(0·11,	0·43)	7	(5,	11)	0·09	(0·07,	0·15)
Western Sub-Saharan Africa	260	(129,	374)	1·32	(0·65,	1·89)	299	(202,	412)	0·82	(0·55,	1·13)
Income category												
High income, OECD	156	(116,	169)	0.17	(0.13,	0.18)	104	(85,	126)	0.10	(0.08,	0.12)
High income, nonOECD	30	(26,	40)	0.16	(0.14,	0.21)	31	(27,	42)	0.15	(0.13,	0.20)
Upper middle income	1,241	(941,	1,433)	0.63	(0.48,	0.73)	1,171	(784,	1,325)	0.47	(0.32,	0.54)
Lower middle income	6,520	(3,582,	8,962)	3.78	(2.08,	5.20)	7,018	(4,228,	8,521)	2.76	(1.66,	3.35)
Low income	797	(471,	1,026)	1.58	(0.93,	2.03)	754	(489,	912)	0.87	(0.56,	1.05)

Table 2: Burden metrics by sex, age, region, and World Bank income group for 2013, including both the absolute numbers of YLDs, YLLs and DALYs (in thousands), and their rates (per 100,000 person-years). 95% uncertainty intervals are given in parentheses.

	YLDs		YLLs		DALYs	
	thousands	**per 100,000**	**thousands**	**per 100,000**	**thousands**	**per 100,000**
Total	565·9	7·84	576·9	7·96	1,142·7	15·81
	(186·4, 1,414·6)	(2·59, 19·61)	(333·0, 701·2)	(4·60, 9·68)	(727·6, 1,978·2)	(10·06, 27·38)
Sex						
Male	268·4	7·33	284·4	7·66	552·7	14·99
	(88·3, 674·9)	(2·41, 18·45)	(153·4, 354·1)	(4·13, 9·52)	(344·9, 946·9)	(9·34, 25·72)
Female	297·5	8·37	292·5	8·29	590·0	16·66
	(98·0, 739·7)	(2·76, 20·81)	(143·2, 370·1)	(4·04, 10·49)	(353·7, 1,042·8)	(9·97, 29·40)
Age						
Post Neonatal	9·6	7·70	56·1	44·95	65·7	52·65
	(3·2, 24·2)	(2·54, 19·41)	(26·1, 77·6)	(20·93, 62·15)	(36·2, 91·7)	(28·98, 73·44)
1 to 4	33·1	6·32	166·0	31·67	199·2	37·99
	(10·5, 84·9)	(2·01, 16·20)	(88·4, 233·1)	(16·85, 44·46)	(123·5, 283·7)	(23·56, 54·12)
5 to 9	70·4	11·34	124·4	20·02	194·8	31·36
	(22·6, 177·1)	(3·64, 28·51)	(55·8, 167·9)	(8·98, 27·02)	(109·7, 309·5)	(17·66, 49·82)
10 to 14	69·0	11·59	52·7	8·86	121·7	20·45
	(22·3, 171·1)	(3·75, 28·74)	(28·7, 64·0)	(4·82, 10·76)	(72·3, 223·8)	(12·14, 37·60)
15 to 19	60·7	10·27	26·1	4·42	86·8	14·69
	(20·1, 151·4)	(3·41, 25·63)	(15·5, 31·1)	(2·62, 5·26)	(46·0, 178·2)	(7·79, 30·16)
20 to 24	53·8	8·77	25·0	4·08	78·8	12·85
	(18·2, 134·4)	(2·97, 21·92)	(17·5, 30·4)	(2·85, 4·96)	(42·7, 161·8)	(6·97, 26·40)
25 to 29	48·7	8·17	26·6	4·46	75·3	12·63
	(16·0, 122·1)	(2·69, 20·47)	(18·7, 32·4)	(3·14, 5·43)	(42·5, 148·5)	(7·13, 24·89)
30 to 34	41·6	7·86	22·9	4·33	64·5	12·19
	(13·4, 103·5)	(2·54, 19·56)	(16·3, 27·6)	(3·09, 5·21)	(36·6, 126·1)	(6·92, 23·84)
35 to 39	36·2	7·39	18·3	3·73	54·5	11·12
	(11·3, 90·8)	(2·30, 18·53)	(13·1, 22·6)	(2·67, 4·61)	(30·0, 108·6)	(6·13, 22·17)
40 to 44	30·5	6·44	15·8	3·34	46·3	9·78
	(9·8, 77·1)	(2·08, 16·29)	(11·9, 19·2)	(2·52, 4·07)	(25·6, 92·6)	(5·41, 19·56)
45 to 49	26·0	5·94	9·3	2·12	35·2	8·05
	(8·6, 65·2)	(1·96, 14·90)	(6·7, 10·5)	(1·54, 2·39)	(17·9, 74·4)	(4·10, 17·02)
50 to 54	23·0	6·04	8·1	2·14	31·1	8·18
	(7·5, 59·1)	(1·97, 15·50)	(5·7, 9·1)	(1·50, 2·40)	(15·9, 67·5)	(4·17, 17·71)
55 to 59	19·0	5·84	6·6	2·05	25·6	7·89
	(6·2, 48·2)	(1·91, 14·86)	(4·8, 7·5)	(1·48, 2·32)	(12·9, 55·0)	(3·97, 16·93)
60 to 64	15·0	5·37	5·9	2·12	21·0	7·49
	(4·9, 37·3)	(1·77, 13·32)	(4·6, 6·8)	(1·63, 2·44)	(11·0, 43·1)	(3·94, 15·40)
65 to 69	10·8	5·74	4·8	2·56	15·6	8·30
	(3·5, 26·9)	(1·88, 14·32)	(3·8, 5·7)	(2·00, 3·03)	(8·4, 31·8)	(4·47, 16·93)
70 to 74	8·0	5·33	3·4	2·28	11·5	7·60
	(2·7, 20·6)	(1·78, 13·65)	(2·5, 4·1)	(1·68, 2·71)	(6·2, 24·0)	(4·12, 15·89)
75 to 79	5·7	5·33	2·1	1·98	7·8	7·30
	(1·9, 14·4)	(1·79, 13·55)	(1·4, 2·4)	(1·35, 2·23)	(4·0, 16·6)	(3·79, 15·57)
80 plus	4·8	4·00	2·5	2·12	7·4	6·12
	(1·6, 12·4)	(1·31, 10·35)	(1·8, 3·1)	(1·48, 2·57)	(4·1, 14·8)	(3·42, 12·30)
Super-region/Region						
Central Europe, Eastern Europe, and Central Asia						
Central Asia	0·9	1·06	1·0	1·06	1·9	2·12
	(0·2, 2·8)	(0·24, 3·23)	(0·8, 1·3)	(0·92, 1·39)	(1·1, 3·7)	(1·27, 4·28)
Central Europe	0·0	0·00	0·6	0·58	0·6	0·58
	(0·0, 0·0)	(0·00, 0·00)	(0·5, 0·9)	(0·48, 1·01)	(0·5, 0·9)	(0·48, 1·01)
Eastern Europe	0·0	0·00	1·0	0·55	1·0	0·55
	(0·0, 0·0)	(0·00, 0·00)	(0·8, 1·4)	(0·43, 0·71)	(0·8, 1·4)	(0·43, 0·71)
High-income						
Australasia	<0·1	0·16	0·1	0·52	0·2	0·67
	(0·0, 0·2)	(0·02, 0·59)	(0·1, 0·2)	(0·33, 0·59)	(0·1, 0·3)	(0·44, 1·11)
High-income	0·2	0·10	0·8	0·53	0·9	0·63
Asia Pacific	(0·0, 0·5)	(0·02, 0·34)	(0·6, 0·9)	(0·38, 0·61)	(0·7, 1·3)	(0·46, 0·90)
High-income	0·5	0·15	1·7	0·52	2·2	0·67
North America	(0·1, 2·0)	(0·01, 0·57)	(1·2, 1·9)	(0·38, 0·62)	(1·5, 3·7)	(0·47, 1·10)
Southern Latin	1·5	2·35	1·1	1·86	2·5	4·20
America	(0·4, 4·0)	(0·62, 6·38)	(0·8, 1·8)	(1·43, 3·06)	(1·4, 5·0)	(2·36, 8·16)
Western Europe	0·0	0·00	1·9	0·51	1·9	0·51
	(0·0, 0·0)	(0·00, 0·00)	(1·4, 2·1)	(0·38, 0·58)	(1·4, 2·1)	(0·38, 0·58)
Latin America and Caribbean						
Andean Latin	4·0	6·98	2·7	4·32	6·7	11·31
America	(1·3, 9·9)	(2·32, 17·17)	(2·1, 3·9)	(3·45, 6·21)	(3·9, 12·5)	(6·45, 21·47)
Caribbean	7·8	17·53	7·6	17·38	15·4	34·91

	(2·7, 19·3)	(6·00, 43·28)	(2·8, 10·2)	(6·28, 23·68)	(8·8, 26·6)	(19·87, 60·18)
Central Latin	23·3	9·33	13·3	5·28	36·6	14·61
America	(8·0, 57·2)	(3·20, 23·00)	(7·6, 16·0)	(3·05, 6·30)	(21·2, 70·8)	(8·47, 28·44)
Tropical Latin	19·4	9·34	11·4	5·74	30·8	15·08
America	(6·6, 48·0)	(3·20, 23·12)	(1·9, 13·8)	(0·91, 7·00)	(15·0, 58·6)	(7·32, 28·47)
North Africa and Middle East						
North Africa	7·4	1·43	4·2	0·76	11·6	2·19
and Middle East	(2·2, 19·7)	(0·42, 3·81)	(3·6, 5·2)	(0·66, 0·94)	(6·3, 24·0)	(1·18, 4·57)
South Asia						
South Asia	220·5	13·20	103·6	6·34	324·2	19·53
	(77·9, 534·7)	(4·68, 31·88)	(82·6, 145·5)	(5·10, 8·71)	(178·8, 622·3)	(10·87, 37·33)
Southeast Asia, East Asia, and Oceania						
East Asia	12·2	0·88	7·3	0·54	19·5	1·41
	(3·4, 34·0)	(0·25, 2·43)	(6·0, 8·3)	(0·44, 0·61)	(10·6, 41·4)	(0·78, 2·98)
Oceania	1·3	11·81	3·8	37·67	5·1	49·48
	(0·4, 3·1)	(4·02, 29·12)	(2·5, 7·3)	(26·81, 65·23)	(3·4, 8·9)	(34·68, 82·81)
Southeast Asia	212·6	33·25	384·1	58·77	596·7	92·02
	(63·9, 557·9)	(10·00, 87·25)	(166·6, 494·0)	(25·56, 75·58)	(342·3, 952·0)	(52·97, 147·61)
Sub-Saharan Africa						
Central Sub-	5·0	4·77	4·6	2·99	9·6	7·76
Saharan Africa	(1·5, 13·0)	(1·44, 12·53)	(2·6, 6·7)	(1·93, 4·24)	(5·4, 17·0)	(4·15, 15·22)
Eastern Sub-	10·6	2·88	3·8	1·05	14·4	3·93
Saharan Africa	(2·7, 30·6)	(0·76, 8·28)	(3·3, 5·0)	(0·79, 1·28)	(6·6, 34·1)	(1·80, 9·21)
Southern Sub-	0·4	0·51	0·4	0·46	0·8	0·97
Saharan Africa	(0·1, 1·2)	(0·13, 1·47)	(0·3, 0·6)	(0·37, 0·77)	(0·4, 1·6)	(0·55, 1·92)
Western Sub-	38·2	10·18	22·0	4·07	60·3	14·25
Saharan Africa	(13·6, 91·2)	(3·64, 24·29)	(13·5, 31·6)	(2·81, 5·48)	(32·9, 117·9)	(7·29, 29·15)
Income category						
High income,	0.6	0.05	4.8	0.45	5.3	0.50
OECD	(0.1, 2.2)	(0.01, 0.21)	(3.7, 5.5)	(0.35, 0.52)	(4.2, 7.2)	(0.40, 0.68)
High income,	0.4	0.20	1.5	0.71	2.0	0.91
nonOECD	(0.1, 1.5)	(0.03, 0.70)	(1.3, 2.0)	(0.60, 0.95)	(1.5, 3.1)	(0.70, 1.46)
Upper middle	87.4	3.53	61.5	2.49	148.9	6.02
income	(28.5, 221.0)	(1.15, 8.93)	(43.2, 71.5)	(1.74, 2.89)	(89.9, 282.2)	(3.63, 11.41)
Lower middle	417.1	16.40	462.1	18.16	879.2	34.56
income	(137.5, 1,038.1)	(5.40, 40.81)	(252.7, 577.4)	(9.94, 22.70)	(560.9, 1,497.6)	(22.05, 58.87)
Low income	59.0	6.81	45.4	5.23	104.4	12.04
	(19.6, 148.5)	(2.26, 17.13)	(29.8, 54.4)	(3.43, 6.27)	(63.5, 197.6)	(7.32, 22.79)

Table 3: Dengue cases (in thousands) and incidence rates (per 100,000 person-years), by sex, age, region, and World Bank income group for 1990 and 2013. 95% uncertainty intervals are given in parentheses.

		1990		2013	
		Cases (thousands)	**Incidence (per 100,000)**	**Cases (thousands)**	**Incidence (per 100,000)**
Total		8,226	148·1	58,419	810·1
		(3,297, 17,246)	(59·4, 310·6)	(23,611, 121,920)	(327·4, 1,690·8)
Sex					
	Male	3,905	139·4	27,637	756·2
		(1,567, 8,181)	(56·0, 292·1)	(11,182, 57,632)	(306·0, 1,577·0)
	Female	4,321	157·3	30,782	865·8
		(1,730, 9,065)	(62·9, 330·1)	(12,429, 64,287)	(349·6, 1,808·2)
Age					
	Post Neonatal	186	152·3	972	778·6
		(75, 389)	(61·3, 318·7)	(393, 2,030)	(314·7, 1,625·3)
	1 to 4	617	121·6	3,322	633·3
		(248, 1,291)	(48·9, 254·4)	(1,342, 6,936)	(255·9, 1,322·2)
	5 to 9	1,255	217·2	7,085	1,140·0
		(504, 2,629)	(87·2, 455·0)	(2,857, 14,808)	(459·8, 2,382·8)
	10 to 14	1,160	220·2	7,001	1,175·6
		(465, 2,431)	(88·3, 461·5)	(2,831, 14,600)	(475·5, 2,451·8)
	15 to 19	963	186·7	6,160	1,041·8
		(385, 2,020)	(74·7, 391·6)	(2,497, 12,827)	(422·2, 2,169·1)
	20 to 24	810	166·6	5,490	894·7
		(324, 1,699)	(66·6, 349·5)	(2,227, 11,421)	(363·0, 1,861·4)
	25 to 29	680	155·1	4,986	834·9
		(272, 1,428)	(62·0, 325·4)	(2,018, 10,392)	(337·9, 1,740·4)
	30 to 34	544	141·4	4,298	811·5
		(218, 1,141)	(56·6, 296·6)	(1,736, 8,973)	(327·7, 1,694·3)
	35 to 39	445	128·3	3,770	768·6
		(179, 933)	(51·5, 268·8)	(1,521, 7,877)	(310·1, 1,605·8)
	40 to 44	323	116·0	3,188	672·6
		(130, 678)	(46·6, 243·2)	(1,283, 6,671)	(270·8, 1,407·4)
	45 to 49	266	117·2	2,730	623·3
		(107, 558)	(47·0, 245·6)	(1,100, 5,712)	(251·1, 1,303·9)
	50 to 54	246	115·8	2,443	640·1
		(99, 517)	(46·4, 242·8)	(985, 5,107)	(258·2, 1,338·2)
	55 to 59	210	113·6	2,038	626·8
		(84, 440)	(45·5, 238·2)	(824, 4,255)	(253·4, 1,308·5)
	60 to 64	177	111·0	1,636	583·5
		(71, 372)	(44·5, 232·8)	(662, 3,414)	(236·1, 1,217·7)
	65 to 69	134	108·5	1,184	629·7
		(54, 282)	(43·5, 227·7)	(479, 2,471)	(254·7, 1,314·1)
	70 to 74	95	110·9	897	593·6
		(38, 200)	(44·3, 233·0)	(363, 1,873)	(240·1, 1,238·9)
	75 to 79	65	102·4	646	605·0
		(26, 136)	(40·7, 215·6)	(261, 1,350)	(244·4, 1,264·3)
	80 plus	48	85·3	573	475·0
		(19, 102)	(33·9, 179·5)	(231, 1,197)	(192·0, 992·9)
Super-region/Region					
Central Europe, Eastern Europe, and Central Asia					
	Central Asia	13	18·5	93	108·3
		(3, 38)	(4·5, 52·5)	(23, 261)	(27·0, 304·5)
	Central Europe	0	0·0	0	0·0
		(0, 0)	(0·0, 0·0)	(0, 0)	(0·0, 0·0)
	Eastern Europe	0	0·0	0	0·0
		(0, 0)	(0·0, 0·0)	(0, 0)	(0·0, 0·0)
High-income					
	Australasia	1	5·4	4	15·3
		(0, 4)	(0·6, 20·5)	(1, 15)	(1·9, 55·4)
	High-income Asia	4	2·5	16	10·2
	Pacific	(1, 13)	(0·4, 8·1)	(3, 50)	(2·0, 31·4)
	High-income	15	5·3	51	14·6
	North America	(2, 56)	(0·6, 20·1)	(6, 190)	(1·7, 54·2)
	Southern Latin	24	49·8	151	242·5
	America	(8, 57)	(16·3, 116·1)	(50, 352)	(80·6, 563·9)
	Western Europe	0	0·0	0	0·0
		(0, 0)	(0·0, 0·0)	(0, 0)	(0·0, 0·0)
Latin America and Caribbean					
	Andean Latin	58	148·1	414	726·4
	America	(24, 121)	(60·3, 307·1)	(171, 855)	(300·3, 1,497·9)

	Caribbean	136 (56, 283)	377·0 (155·6, 782·6)	811 (340, 1,665)	1,823·4 (765·0, 3,742·9)
	Central Latin America	335 (141, 685)	194·6 (82·2, 397·9)	2,406 (1,021, 4,890)	970·2 (411·7, 1,972·3)
	Tropical Latin America	307 (131, 621)	196·4 (83·9, 397·5)	2,019 (867, 4,064)	973·7 (417·9, 1,959·8)
North Africa and Middle East					
	North Africa and Middle East	97 (34, 219)	29·8 (10·5, 67·2)	764 (273, 1,713)	148·5 (53·2, 332·9)
South Asia					
	South Asia	3,218 (1,389, 6,436)	285·3 (123·1, 570·5)	22,851 (9,941, 45,549)	1,379·1 (600·1, 2,748·6)
Southeast Asia, East Asia, and Oceania					
	East Asia	183 (61, 425)	15·2 (5·1, 35·2)	1,258 (432, 2,895)	89·6 (30·7, 206·2)
	Oceania	18 (7, 37)	272·2 (110·9, 563·7)	128 (54, 264)	1,226·2 (510·9, 2,519·8)
	Southeast Asia	3,188 (1,180, 6,958)	682·2 (252·7, 1,488·3)	21,841 (8,073, 47,725)	3,432·6 (1,269·3, 7,497·8)
Sub-Saharan Africa					
	Central Sub-Saharan Africa	55 (20, 121)	105·2 (38·6, 231·3)	515 (190, 1,124)	503·6 (186·4, 1,099·2)
	Eastern Sub-Saharan Africa	118 (37, 283)	62·9 (19·9, 150·4)	1,091 (349, 2,597)	300·9 (96·3, 715·9)
	Southern Sub-Saharan Africa	6 (2, 16)	11·4 (3·4, 27·6)	42 (13, 103)	52·8 (15·9, 127·5)
	Western Sub-Saharan Africa	448 (192, 905)	223·7 (95·7, 451·9)	3,963 (1,701, 7,977)	1,071·9 (460·3, 2,157·3)
Income category					
	High income, OECD	17 (2, 67)	1.9 (0.2, 7.3)	60 (7, 225)	5.7 (0.7, 21.3)
	High income, nonOECD	12/ (2, 40)	6.3 (1.0, 21.1)	47 (8, 150)	22.1 (4.0, 70.2)
	Upper middle income	1,469 (589, 3,152)	74.7 (29.9, 160.3)	9,795 (3,958, 20,949)	395.9 (160.0, 846.8)
	Lower middle income	6,541 (2,652, 13,955)	379.2 (153.7, 809.0)	46,653 (19,053, 99,229)	1,833.9 (749.0, 3,900.7)
	Low income	851 (347, 1,814)	168.3 (68.6, 358.8)	6,616 (2,684, 14,150)	763.2 (309.6, 1,632.1)

Figure Legends

Figure 1: Age-standardized mortality rates from dengue (per million person-years), by country, in 2013.

Figure 2: Age-standardized incidence rates of dengue (per 100,000 person-years), by country, in 2013.

Figure 3: Percent change in dengue DALYs from 1990, among dengue endemic countries (i.e. those with a non-zero probability of dengue transmission based on Bhatt et al[7]), globally and by GBD super-region.

Contributors

JDS, DSS, YAH, EAU, LEC, OJB, and SIH prepared the first draft. All other authors provided critical feedback and edits to finalize the manuscript. JDS performed the final statistical analyses and prepared all tables and figures. CJLM conceived of the study and provided overall guidance. All other authors provided data, review results, provided guidance on methodology, and reviewed the manuscript.

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Ethics committee approval

There were no human subjects involved in this research.

Figure 1

Dengue mortality per million, 2013

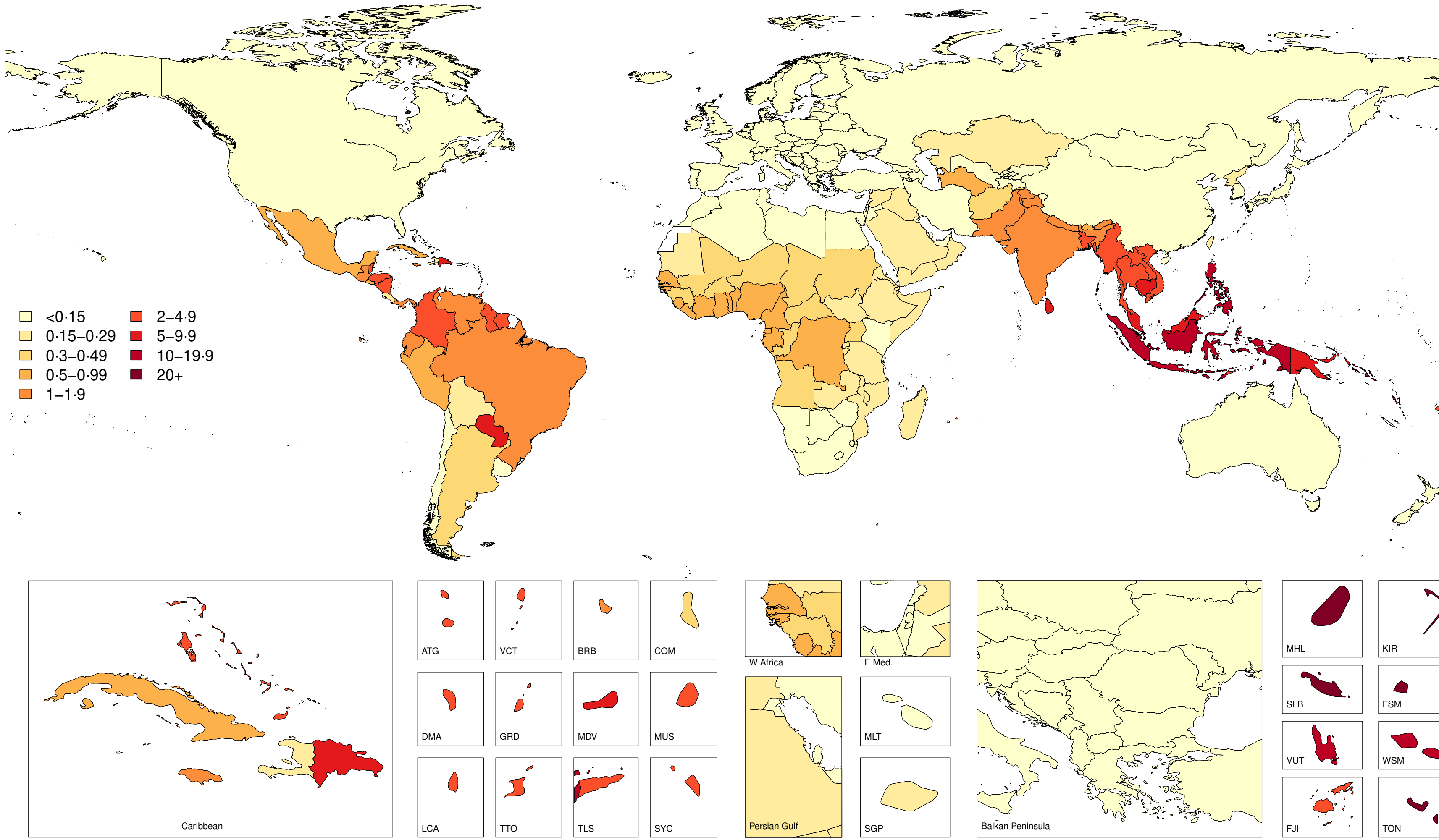


Figure 2

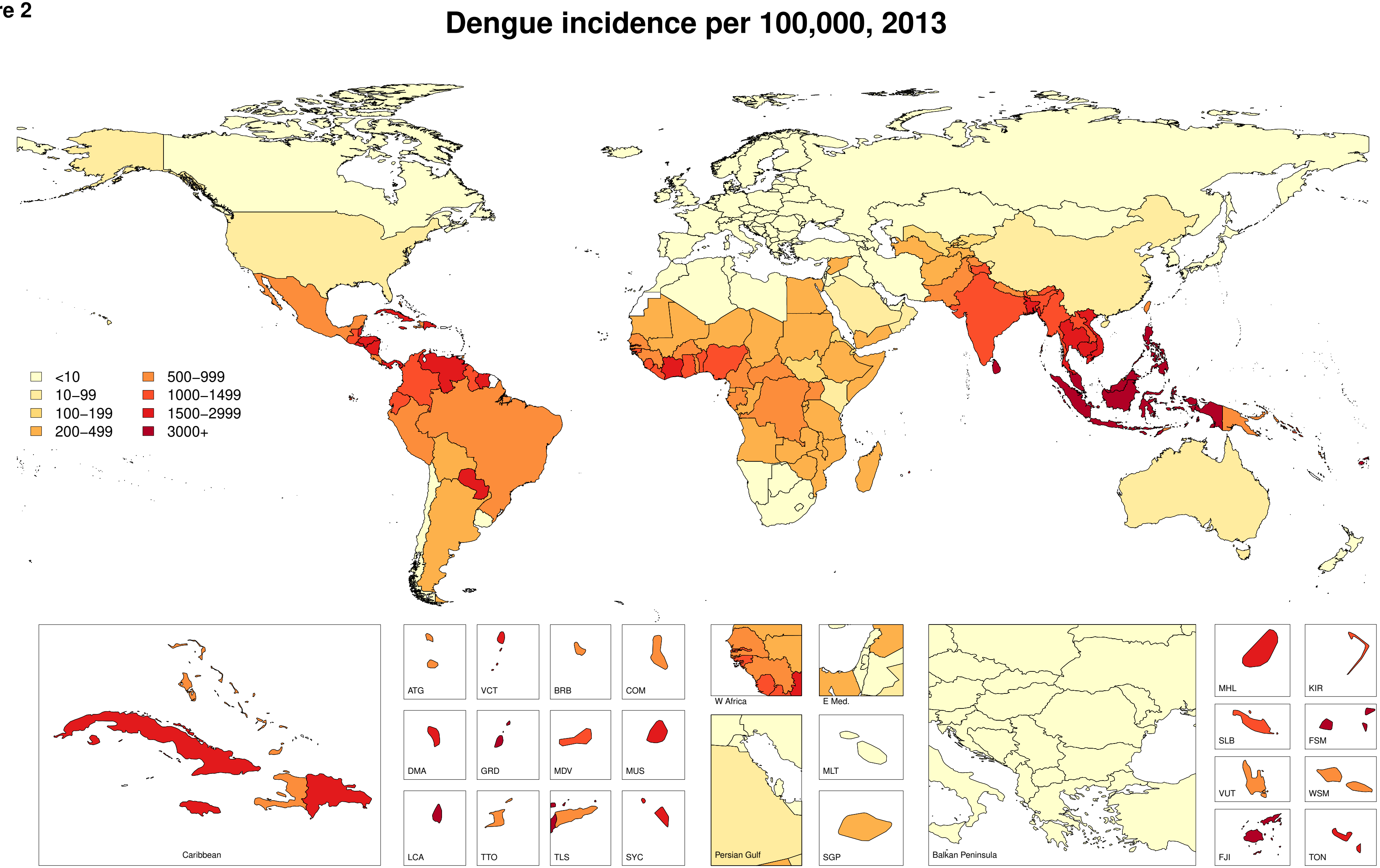
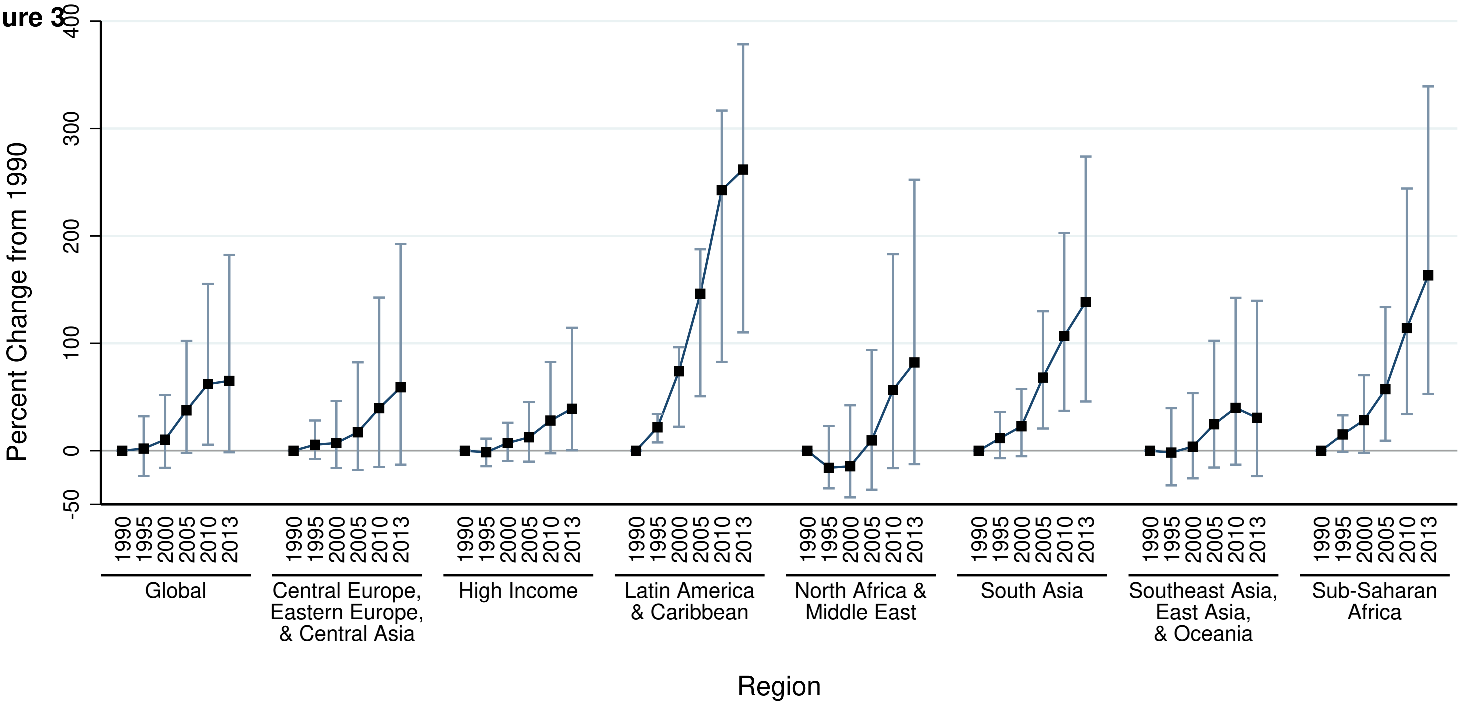

Dengue incidence per 100,000, 2013
<10
10–99
100–199
200–499
500–999
1000–1499
1500–2999
3000+
Caribbean
ATG
VCT
BRB
COM
DMA
GRD
MDV
MUS
LCA
TTO
TLS
SYC
W Africa
E Med.
Persian Gulf
MLT
SGP
Balkan Peninsula
MHL
KIR
SLB
FSM
VUT
WSM
FJI
TON

Figure 3


Percent Change from 1990
400
300
200
100
0
-50
1990 1995 2000 2005 2010 2013
Global
Central Europe, Eastern Europe, & Central Asia
High Income
Latin America & Caribbean
North Africa & Middle East
South Asia
Southeast Asia, East Asia, & Oceania
Sub-Saharan Africa
Region